

REMARKS/ARGUMENTS

Reconsideration of this application is requested. Claims 1-22 are in the case.

Claims 1-12, 15-18 and 22 stand rejected under 35 U.S.C. §103(a) as allegedly unpatentable over U.S. Patent 4,789,733 to Winkelman in view of U.S. Patent 5,605,887 to Pines et al. The rejection is respectfully traversed.

The invention of the present application is directed to a method of obtaining a fibrinogen enriched preparation. The method comprises the steps of:

- (i) adding an effective amount of a sulphated polysaccharide (SPS) to a fibrinogen containing solution to form a precipitate containing fibrinogen; and
- (ii) extracting fibrinogen from the precipitate containing fibrinogen from step (i) with a solution containing at least 0.1M salt to obtain a fibrinogen enriched preparation.

As conceded by the Examiner, Winkelman does not expressly teach a method for extracting fibrinogen from a heparin-precipitate using a solution containing at least 0.1 M salt. Thus, it is clear that Winkelman does not disclose or suggest the second step of the method of the present invention of extracting fibrinogen from the precipitate containing fibrinogen from step (i) with a solution containing at least 0.1M salt to obtain a fibrinogen enriched preparation.

In an attempt to cure the deficiencies of Winkelman, the Examiner relies on Pines *et al.* for an alleged teaching of a fibrinogen extraction buffer (i.e. use of a salt solution to extract fibrinogen from the precipitate to obtain a fibrinogen enriched preparation). However, as conceded by the Examiner, Pines *et al.* uses a PEG-1000 solution instead of heparin to produce the precipitate containing fibrinogen (see: Example 1 of Pines *et*

al.). In other words, Pines *et al.* does not disclose or suggest the first essential feature of the present invention (namely: "adding an effective amount of **sulphated polysaccharide (SPS)** to a fibrinogen containing solution to form a precipitate containing fibrinogen").

Based on these two completely separate documents, the Examiner concludes that it would have been obvious to a person of ordinary skill to combine the disclosures of Winkelman and Pines *et al.* and use the extraction buffer of Pines *et al.* to extract fibrinogen the a heparin precipitate described by Winkelman. This position is respectfully traversed.

The standard to be applied in evaluating obviousness in the recent case of *In re Rouffet*, 47 USPQ 2d 1453 (Fed. Cir. 1998):

"To prevent the use of hindsight based on the invention to defeat patentability of the invention, this Court requires the examiner to show a motivation to combine the references that create the case of obviousness. In other words, the examiner **must show reasons** that the skilled artisan, confronted with the same problems as the inventor and with no knowledge of the claimed invention, would select the elements from the cited prior art references for combination in the manner claimed." 47 USPQ 2d at 1457 1458. (Emphasis added)

The case is also consistent with other CAFC cases:

"Obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention, **absent some teaching, suggestion or incentive supporting the combination**. *In re Geiger*, 815 F. 2d 686 (Fed. Cir. 1987) at 688, 2 USPQ 2d 1276 at 1278, citing ACS Hospital Systems Inc. v. Montefiore Hospital, 732 F. 2d 1572 (Fed. Cir. 1984) at 1577, 221 USPQ 929 at 933." (Emphasis added)

In the present case, the Examiner has not shown any motivation for one of ordinary skill in this art to combine the cited references, and has certainly not shown how one could derive the invention as now claimed even if the references were

combined (it is believed that the references would not have been combined by one of ordinary skill). The Examiner appears to take the position that any disclosure describing the purification of fibrinogen or FVIII can be combined to arrive at the present invention. This is not the standard to be applied. Moreover, the Examiner has applied an improper hindsight analysis of the method of the invention when looking for prior art documents to combine.

First, it is important to bear in mind that Winkelman is directed to a process for preparing purified FVIII. There would have been no reason for a person skilled in the art wishing to purify fibrinogen to consult this reference.

Secondly, there would have been no motivation for a person of ordinary skill to combine the disclosures Winkelman and Pines *et al.* Pines *et al.* clearly discloses that the nature of the material used to form the fibrinogen containing precipitate has an effect on how the fibrinogen extraction process proceeds (see column 10, lines 55 to 63). In this passage, Pines *et al.* clearly describes that the use of PEG-1000 is preferable to the use of higher polyethylene glycols (e.g. PEG-8000). In other words, even variations in the type of PEG used affects the resulting extraction process. In light of this disclosure, there would have been no reason to expect that a buffer composition suitable for extraction of fibrinogen from a PEG precipitate could be used to extract fibrinogen from a heparin precipitate.

Withdrawal of the obviousness rejection based on Winkelman and Pines *et al* is believed to be in order. Such action is respectfully requested.

KANELLOS et al
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Claims 1, 13, 14 and 19-21 stand rejected under 35 USC 103(a) as allegedly unpatentable over Winkelman and Pines *et al.* in further view of Altieri *et al.* The Examiner's allegation is respectfully traversed.

As argued above, the combination of Winkelman and Pines *et al.* is clearly impermissible and, in any event, does not lead to the presently claimed invention. The deficiencies of the Winkelman and Pines *et al* are not cured by the addition of Altieri *et al.* Altieri et al is relied upon for an alleged disclosure relating to the use of a Sepharose 4B column, but is otherwise irrelevant to the invention as claimed.

In summary, one of ordinary skill would not have motivated to arrive at the presently claimed invention based on the combined references relied on by the Examiner in the outstanding action. Absent any such motivation, a *prima facie* case of obviousness has not been generated in this case. Reconsideration and withdrawal of the obviousness rejections are accordingly respectfully requested.

Allowance of the application is awaited.

Respectfully submitted,

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